L7 ANSWER 12 OF 12 USPATFULL on STN
AN 1998:157464 USPATFULL
TI Cytolytic bradykinin antagonists
IN Stewart, John M., Denver, CO, United States
Chan, Daniel C., Denver, CO, United States
Whalley, Eric T., Golden, CO, United States
Gera, Lajos, Denver, CO, United States
PA University of Colorado, Boulder, CO, United States (U.S. corporation)
Cortech, Inc., Denver, CO, United States (U.S. corporation)
PI US 5849863 19981215
AI US 1995-526065 19950908 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Delaney, Patrick R.
LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 944
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:

. . . A bradykinin antagonist compound of the general formula: BKA.sub.1 --X--BKA.sub.2, wherein BKA.sub.1 and BKA.sub.2 are independently selected from the following: **Arg-Pro-Pro** -Gly-Phe-Ser-Pro-Phe-Arg (SEQ ID NO:1); DArg-Arg-Pro-Hyp-Gly-Thi-Ser-DTic-Nig-Arg; DArg-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Oic-Arg; Cys-DArg-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Oic-Arg; .epsilon.-Lys-DArg-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Oic-Arg; Gun-Gly-8-Lys-**Arg-Pro-Pro**-Gly-Phe-Ser-Pro-Leu (SEQ ID NO:2); Dhq-DArg-Arg-Pro-Hyp-Gly-.epsilon.-Lys-Ser-DCpg-CPg-Arg; Dhq-.epsilon.-Lys-DArg-Arg-Pro-Hyp-Gly-Cpg-Ser-DCpg-CPg-Arg; DArg-Arg-Pro-Hyp-Gly-Cpg-Ser-DCpg-CPg; DArg-Cys-Pro-Hyp-Gly-Cpg-Ser-DCpg-Cpg; DArg-Lys-Pro-Hyp-Gly-Cpg-Ser-DCpg-Cpg; DArg-Arg-Pro-Hyp-Gly-Cpg-Ser-Tic-Cpg; DArg-Arg-Pro-Hyp-Gly-Thi-Ser-Tic-Cpg; DArg-Arg-Pro-Hyp-Gly-Cpg-Ser-DTic-Cpg; DArg-Arg-Pro-Hyp-Gly-Thi-Ser-DTic-Cpg; DArg-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Oic; Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Leu; DArg-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Leu; Gun- DArg-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Oic; DArg-Arg-Pro-Hyp-Gly-Thi-Ser-DIgl-Oic; Gun-DArg-Arg-Pro-Hyp-Gly-Thi-Ser-DIgl-Oic; DArg-Arg-Pro-Hyp-Gly-Igl-Ser-DTic-Cpg; Lys-Arg-Pro-Hyp-Gly-Igl-Ser-DTic-Cpg; Lys-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Oic; Lys- Lys-Arg-Pro-Hyp-Gly-Igl-Ser-DIgl-Oic; and DArg-Arg-Pro-Hyp-Gly-Thi-Ser-DTic-Oic; and X is a **linker** group.

ANSWER 7 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1997-065304 [06] WPIDS

DNC C1997-021492

TI Inhibition of platelet activation and aggregation - by admin. of new or known bradykinin analogues.

DC B04

IN HASAN, A A K; SCHMAIER, A H

PA (UNMI) UNIV MICHIGAN

CYC 71

PI WO 9641640 A1 19961227 (199706)* EN 73p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SI SK TJ TM TR TT UA US UZ VN
AU 9663828 A 19970109 (199717)
EP 871464 A1 19981021 (199846) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 703256 B 19990325 (199924)
US 6143719 A 20001107 (200059)
JP 2001511762 W 20010814 (200154) 76p
EP 871464 B1 20030402 (200325) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69627191 E 20030508 (200338)

ADT WO 9641640 A1 WO 1996-US9940 19960607; AU 9663828 A AU 1996-63828 19960607; EP 871464 A1 EP 1996-923268 19960607, WO 1996-US9940 19960607; AU 703256 B AU 1996-63828 19960607; US 6143719 A Provisional US 1995-96P 19950609, WO 1996-US9940 19960607, US 1996-676242 19960716; JP 2001511762 W WO 1996-US9940 19960607, JP 1997-503243 19960607; EP 871464 B1 EP 1996-923268 19960607, WO 1996-US9940 19960607; DE 69627191 E DE 1996-627191 19960607, EP 1996-923268 19960607, WO 1996-US9940 19960607

FDT AU 9663828 A Based on WO 9641640; EP 871464 A1 Based on WO 9641640; AU 703256 B Previous Publ. AU 9663828, Based on WO 9641640; US 6143719 A Based on WO 9641640; JP 2001511762 W Based on WO 9641640; EP 871464 B1 Based on WO 9641640; DE 69627191 E Based on EP 871464, Based on WO 9641640

PRAI US 1995-96P 19950609; US 1996-676242 19960716

AB WO 9641640 A UPAB: 19970205

Methods for (a) inhibiting thrombin-induced activation of platelets or other cells, (b) preventing platelet aggregation and (c) inhibiting ADP-induced platelet activation comprise admin. of a peptide (I) having an amino acid sequence of formula X1-**Arg**-**Pro**-**Pro**-Gly-X2 or a multimer (II) of formula L(X1-**Arg**-**Pro**-**Pro**-Gly-X2)n, where: X1 and X2 = 0-30 natural or synthetic amino acids; L = a **linker** comprising a covalent bond or a chemical gp.; and n = 2-20; provided that the peptide is not native bradykinin. Also claimed is a method for inhibiting thrombin-induced activation of platelets or other cells, comprising admin. of a peptide (III) having the sequence (D-Arg)-Arg-Pro-Hyp-Gly-Thi-Ser-(D-Tic)-Oic-Arg. Two specific peptides (II) are claimed as new.

USE -The methods and peptides are used to prevent arterial occlusions arising from coronary thrombosis and stroke.

ADVANTAGE - (I)-(II) are bradykinin analogues that inhibit alpha-thrombin- and ADP-induced platelet activation and secretion, inhibit alpha-thrombin-induced Ca mobilisation and prevent alpha-thrombin from cleaving its platelet receptor.

Dwg.0/11

=>

```
=> s arg pro pro and linker
          2   FILE BIOSIS
          3   FILE BIOTECHABS
          3   FILE BIOTECHDS
          2   FILE CAPLUS
         14   FILE DGENE
          2   FILE EMBASE
          2   FILE ESBIOBASE
          4   FILE IFIPAT
          2   FILE MEDLINE
  46 FILES SEARCHED...
          2   FILE SCISEARCH
          1   FILE TOXCENTER
       1347   FILE USPATFULL
         24   FILE USPAT2
          5   FILE WPIDS
          5   FILE WPINDEX

  15 FILES HAVE ONE OR MORE ANSWERS,    67 FILES SEARCHED IN STNINDEX

L4   QUE ARG PRO PRO AND LINKER
```

YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-619260 [66] WPIDS
DNN N2002-490177 DNC C2002-175014
TI New chimeric bifunctional molecules that target specific cells and regulate the apoptosis function of the permeability transition pore complex of the mitochondria, useful for treating or preventing e.g. cancer or ischemia.
DC B04 D16 S03
IN BRIAND, J; EDELMAN, L; JACOTOT, E D F; JACOTOT, E
PA (BRIA-I) BRIAND J; (EDEL-I) EDELMAN L; (JACO-I) JACOTOT E D F; (CNRS) CENT NAT RECH SCI; (INSP) INST PASTEUR
CYC 100
PI WO 2002061105 A2 20020808 (200266)* EN 76p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003077826 A1 20030424 (200330)
ADT WO 2002061105 A2 WO 2002-EP1633 20020201; US 2003077826 A1 Provisional US 2001-265594P 20010202, US 2002-59261 20020131
PRAI US 2001-265594P 20010202; US 2002-59261 20020131
TECH UPTX: 20021014
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Molecule: The chimeric molecule modulates the activity of the PTPC of a eukaryotic cell by regulating the opening or closing of the pore. The second functional molecule of the chimera regulates the apoptosis activity linked to the PTPC of the specific cells. The second functional molecule also interacts specifically with the ANT of the PTPC of the mitochondria, particularly to ANT isoforms 1, 2 or 3. The chimeric molecule has the formula (I) or (II):
Targ-Tox (I);
Targ-Save (II).
Targ = an antibody, antibody fragment, recombinant antibody fragment, M350/ScFv, V461/ScFv, homing peptide, or any of ANTENNAPEDIA third helix, HIV-1 V pr 83-96 transduction domain, HIV-1 Tat48-59 transduction domain, HIV-1 Tat49-57 transduction domain or pep-1;
Tox = a viral or a retroviral apoptotic peptide or peptidomimetic, or a fragment of a protein that interacts with PTPC of a specific eukaryotic cell to cause apoptosis of the cell; and
Save = a viral or retroviral or cellular antiapoptotic peptide or peptidomimetic, or a fragment of protein that interacts with PTPC of a specific eukaryotic cell to prevent apoptosis of the cell; provided that when Save is a viral peptide, then Save is not vMIA protein Cytomegalovirus.
The ANTENNAPEDIA third helix, HIV-1 V pr 83-96 transduction domain, HIV-1 Tat48-59 transduction domain, HIV-1 Tat49-57 transduction domain or pep-1 has the following sequences: ANTENNAPEDIA third helix: Arg-Gln-Ile-Lys-Ile-Thr-Phe-Gln-Asn-Arg-Arg-Met-Lys-Thr-Lys-Lys; HIV-1 V pr 83-96 transduction domain: Ile-Ile-Gln-Gln-Arg-Arg-Thr-Arg-Asn-GAla-Ser-Lys-Ser; HIV-1 Tat48-59 transduction domain: Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-**Arg-Pro-Pro**; HIV-1 Tat49-57 transduction domain: Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg; pep-1: Lys-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu-Trp. Preferably, Tox is a D-peptide, a psi-peptide or a retro-inverso peptide chosen from any of 35 peptidic sequences, e.g.: Vpr71-82: His-Phe-Arg-Ile-Gly-Cys-Arg-His-Ser-Arg-Ile-Gly; Mastoparan Vespula Lewisii: Ile-Asn-Leu-Lys-Ala-Leu-Ala-Ala-

Leu-Ala-Lys-Lys-Ile-Leu; HNUR77 (555-568): Leu-Ser-Arg-Leu-Leu-GLys-Leu-Pro-Glu-Leu-Arg-Thr-Leu; Bid(84-100): Arg-Asn-Ile-Ala-Arg-His-Leu-Ala-Gln-Val-Gly-Asp-Ser-Met-Arg-Asp-Arg; Bax(57-72): Lys-Lys-Leu-Ser-Glu-Cys-Leu-Lys-Arg-Ile-Gly-Asp-Glu-Leu-Asp-Ser; HBX(70-78): Ala-Leu-Arg-Phe-Thr-Ser-Ala-Arg-Arg; DCC(1376-1390): Lys-Thr-His-Val-Lys-Thr-Ala-Ser-Leu-Gly-Leu-Ala-Gly-Lys-Ala; ANT1(104-116): Asp-Arg-His-Lys-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn; Bad103-127: Asn-Leu-Trp-Ala-Ala-Gln-Arg-Tyr-Gly-Arg-Glu-Leu-Arg-Arg-Met-Ser-Asp-Glu-Phe-Val-Asp-Ser-Phe-Lys-Lys; or Bax52-76: Gln-Asp-Ala-Ser-Thr-Lys-Lys-Leu-Ser-Glu-Cys-Leu-Lys-Arg-Ile-Gly-Asp-Glu-Leu-Asp-Ser-Asn-Met-Glu-Leu. Save is preferably a L-peptide, a D-peptide or a retro-inverso peptide chosen from the following peptidic sequences: ANT1(104-116): Asp-Arg-His-Lys-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn; ANT2(104-116): Asp-Lys-Arg-Thr-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn; ANT3(104-116): Asp-Lys-His-Thr-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn; ANT1,2,3(117-134): Leu-Ala-Ser-Gly-Gly-Ala-Ala-Gly-Ala-Thr-Ser-Leu-Cys-Phe-Val-Tyr-Pro-Leu; ANT1(104-134): Asp-Arg-His-Lys-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn-Leu-Ala-Ser-Gly-Gly-Ala-Ala-Gly-Ala-Thr-Ser-Leu-Cys-Phe-Val-Tyr-Pro-Leu; ANT1(104-134): Asp-Lys-Arg-Thr-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn-Leu-Ala-Ser-Gly-Gly-Ala-Ala-Gly-Ala-Thr-Ser-Leu-Cys-Phe-Val-Tyr-Pro-Leu; or ANT1(104-134): Asp-Lys-His-Thr-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn-Leu-Ala-Ser-Gly-Gly-Ala-Ala-Gly-Ala-Thr-Ser-Leu-Cys-Phe-Val-Tyr-Pro-Leu. Preferably, the Targ and Tox peptides, or the Targ and Save peptides are covalently bonded through a peptide **linker** comprising 3-18 amino acids. The chimeric molecule comprises a mitochondrial localization sequence (MLS), which has the function of addressing specifically the second functional molecule to mitochondrial membranes or intermembrane space.

Preferred Method: In (M2), determining the presence of a cancer cell having a tumor-associated antigen on its surface in a biological sample comprises:

(a) contacting a biological sample with the chimeric peptide molecule to permit the binding between the chimeric peptide and the antigen on the surface of the cancer cell;

(b) detecting the binding by standard techniques; and

(c) optionally quantifying the binding detected in step (b).

In (M3), inducing death by apoptosis in a tumoral or viral infected cell having a tumor-associated antigen on its surface comprises contacting a biological sample with the chimeric peptide molecule to permit the binding between the chimeric peptide and the antigen on the surface of the cancer, and to allow the entry inside the cell and induce death of the cell by apoptosis. In (M4), preventing cell death by mitochondrial apoptosis comprises contacting a biological sample with the chimeric molecule to permit binding between the chimeric molecule and the cell, and to allow the entry inside the cell and prevent cell death by apoptosis. In (M5), identifying an active agent that interacts with the activity of the PTPC comprises:

(a) contacting a biological sample containing cells with PTPC with the chimeric peptide in the presence of a candidate agent;

(b) comparing the binding of the chimeric peptide with the PTPC in the absence of the agent; and

(c) optionally, testing the activity of the selected agent on a preparation of a cellular extract comprising subcellular elements with the PTPC.

In (M6), identifying an active agent that interacts with the ANT peptide of PTPC comprises:

(a) contacting a biological sample containing cells with the ANT peptide of PTPC with the chimeric peptide in the presence of a candidate agent; and

(b) comparing the binding of the chimeric peptide with the ANT in the absence of the agent; and

(c) optionally, testing the activity of the selected agent on a preparation of a cellular extract comprising subcellular elements with the

ANT peptide of the PTPC.

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
AN 2002:355706 CAPLUS
DN 137:135201
TI Bradykinin-related compounds as new drugs for cancer and inflammation
AU Stewart, John M.; Gera, Lajos; Chan, Daniel C.; Bunn, Paul A., Jr.; York, Eunice J.; Simkeviciene, Vitalija; Helfrich, Barbara
CS Department of Biochemistry, University of Colorado School of Medicine, Denver, CO, 80262, USA
SO Canadian Journal of Physiology and Pharmacology (2002), 80(4), 275-280
CODEN: CJPPA3; ISSN: 0008-4212
PB National Research Council of Canada
DT Journal
LA English
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Bradykinin (BK) (**Arg-Pro-Pro**-Gly-Phe-Ser-Pro-Phe-Arg) is an important growth factor for small-cell lung cancer (SCLC) and prostate cancer (PC). These cancers have cells of neuroendocrine origin and express receptors for a variety of neuropeptides. BK receptors are expressed on almost all lung cancer cell lines and on many PC cells. The authors' very potent BK antagonist B9430 (D-Arg-Arg-Pro-Hyp-Gly-Igl-Ser-D-Igl-Oic-Arg) (Hyp, trans-4-hydroxy-L-proline; Igl, .alpha.-2-indanylglycine; Oic, octahydroindole-2-carboxylic acid) is a candidate anti-inflammatory drug but does not inhibit growth of SCLC or PC. When B9430 is dimerized by N-terminal crosslinking with a suberimide **linker**, the product B9870 is a potent growth inhibitor for SCLC both in vitro and in vivo in athymic nude mice. Daily i.p. injection at 5 mg/kg/day beginning on day 8 after SCLC SHP-77 cell implantation gave 65% inhibition of tumor growth. B9870 stimulates apoptosis in SCLC by a novel "biased agonist" action. The authors have also developed new small mimetic antagonists. BKM-570 (F5C-OC2Y-Atmp) (F5C, pentafluorocinnamic acid; OC2Y, O-2,6-dichlorobenzyl tyrosine; Atmp, 4-amino-2,2,6,6-tetramethylpiperidine) is very potent for inhibition of SHP-77 growth in nude mice. When injected daily i.p. at 5 mg/kg, M-570 gave 90% suppression of tumor growth. M-570 is more potent than the well-known anticancer drug cisPlatin (60% inhibition) or the recently developed SU5416 (40% inhibition) in this model. M-570 also showed activity against various other cancer cell lines in vitro (SCLC, non-SCLC, lung, prostate, colon, cervix) and inhibited growth of prostate cell line PC3 in nude mice. M-570 and related compds. evidently act in vivo through pathways other than BK receptors. These compds. have clin. potential for treatment of human lung and prostate cancers.

L6 ANSWER 3 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-205862 [18] WPIDS
DNC C2000-063579
TI Method of imaging cells or tissues such as thrombus, particularly deep venous thrombosis and pulmonary embolism comprising using novel radiolabeled fibrin-alpha-chain peptides.
DC B04 K08
IN THAKUR, M L
PA (UYJE-N) UNIV JEFFERSON THOMAS
CYC 22
PI WO 2000009076 A2 20000224 (200018)* EN 28p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 1105164 A2 20010613 (200134) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002522778 W 20020723 (200263) 29p
ADT WO 2000009076 A2 WO 1999-US19011 19990817; EP 1105164 A2 EP 1999-966745

19990817, WO 1999-US19011 19990817; JP 2002522778 W WO 1999-US19011 19990817, JP 2000-564580 19990817

FDT EP 1105164 A2 Based on WO 200009076; JP 2002522778 W Based on WO 200009076

PRAI US 1998-96803P 19980817

AB WO 200009076 A UPAB: 20000706

NOVELTY - Compositions (I) or (II) for radiolabeling agents that bind to fibrin, are new.

DETAILED DESCRIPTION - Composition of formula (I) or (II) is new.

X1-P-X2-Z-M (I)

M-Z-X2-P-X1 (II)

Where:

X1 and X2 = 0-20 natural or synthetic amino acids;

P = peptide comprising Gly Pro Arg (III) or one of its analogs or fragments;

Z = **linker** comprising one or more natural or synthetic amino acids;

M = radiolabeling moiety consisting of a chelating moiety capable of complexing with a selected radionuclide.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of imaging mammalian cells or tissue by administering the above composition to a mammal at a target site and detecting it; and

(2) a method of imaging a thrombus in a mammal by administering a composition with a radiolabeling moiety and which binds to fibrin and detecting the composition at the thrombus site.

USE - The composition is used to image mammalian cells or tissues, preferably thrombus (claimed), particularly deep venous thrombosis (DVT) and pulmonary embolism (PE).

ADVANTAGE - In experiments Tc-99m-TP 850, a composition of the invention, had considerably higher radioactivity uptake on PE than at least two activated specific Tc-99m labeled peptides previously evaluated. With Tc-99m-Tp 850, all PE were detectable except those that had lysed spontaneously at 48 hours post placement. The disappearance of 48 hour old clots was confirmed by the loss of X-ray opacity of these clots.

Dwg.0/6

TECH UPTX: 20001114

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Moiety: The radiolabeling moiety is complexed to a radionuclide which is preferably technetium-99m. The composition is preferably Tc-99m-TP850, where TP 850 is the decapeptide, Gly-Pro-**Arg-Pro-Pro**-Aba-Gly-Gly-(D)-Ala-Gly (IV) (Aba is 4-aminobutyric acid). The composition preferably comprises (IV). M comprises Gly-(D)Ala-Gly-Gly (V) as a chelating moiety for a radionuclide.

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2

AN 2000:394598 CAPLUS

DN 133:208174

TI Synthesis of different types of dipeptide building units containing N- or C-terminal arginine for the assembly of backbone cyclic peptides

AU Schumann, C.; Seyfarth, L.; Greiner, G.; Reissmann, S.

CS Friedrich-Schiller-Universitat Jena, Institut fur Biochemie und Biophysik, Jena, D-07743, Germany

SO Journal of Peptide Research (2000), 55(6), 428-435
CODEN: JPERFA; ISSN: 1397-002X

PB Munksgaard International Publishers Ltd.

DT Journal

LA English

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Different types of dipeptide building units contg. N- or C-terminal arginine were prepd. for synthesis of the backbone cyclic analogs of the peptide hormone bradykinin (BK: **Arg-Pro-Pro**-Gly-Phe-Ser-Pro-Phe-Arg). For cyclization in the N-terminal sequence,

N-carboxyalkyl and N-aminoalkyl functionalized dipeptide building units were synthesized. To avoid lactam formation during the condensation of the N-terminal arginine to the N-alkylated amino acids at position 2, the guanidino function has to be deprotected. Best results were obtained by coupling Z-Arg(Z)2-OH with [(Me2N)2CF]PF6/collidine in CH2Cl2. Another dipeptide building unit with an acylated reduced peptide bond contg. C-terminal arginine was prepd. to synthesize BK-analogs with backbone cyclization in the C-terminus. To achieve complete condensation to the resin and to avoid side-reactions during activation of the arginine residue, this dipeptide unit was formed on a hydroxycrotonic acid **linker**. HYCRAM technol. was applied using the Boc-Arg(Alloc)2-OH deriv. and the Fmoc group to protect the aminoalkyl function. The reduced peptide bond was prepd. by reductive alkylation of the arginine deriv. with the Boc-protected amino aldehyde, derived from Boc-Phe-OH. The best results for condensation of the branching chain to the reduced peptide bond were obtained using mixed anhydrides. Both types of dipeptide building units can be used in solid-phase synthesis in the same manner as amino acid derivs.

L6 ANSWER 5 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1998-583390 [49] WPIDS
DNC C1998-174559
TI Inhibition of thrombin-induced platelet or other cell activation - comprises administering compound with amino acid segments of specific sequences, used for preparation of therapeutics.
DC B04 B05
IN HASAN, A A K; SCHAMAIER, A H; SCHMAIER, A H
PA (UNMI) UNIV MICHIGAN
CYC 81
PI WO 9847522 A1 19981029 (199849)* EN 55p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA US UZ VN
AU 9872528 A 19981113 (199913)
EP 1019070 A1 20000719 (200036) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 734935 B 20010628 (200142)
JP 2001518119 W 20011009 (200174) 58p
AU 2001077299 A 20011213 (200210)#
ADT WO 9847522 A1 WO 1998-US8015 19980421; AU 9872528 A AU 1998-72528 19980421; EP 1019070 A1 EP 1998-919827 19980421, WO 1998-US8015 19980421; AU 734935 B AU 1998-72528 19980421; JP 2001518119 W JP 1998-546274 19980421, WO 1998-US8015 19980421; AU 2001077299 A Div ex AU 1998-72528 19980421, AU 2001-77299 20010928
FDT AU 9872528 A Based on WO 9847522; EP 1019070 A1 Based on WO 9847522; AU 734935 B Previous Publ. AU 9872528, Based on WO 9847522; JP 2001518119 W Based on WO 9847522; AU 2001077299 A Div ex AU 734935
PRAI US 1997-46085P 19970423; AU 2001-77299 20010928
AB WO 9847522 A UPAB: 19981210
Inhibiting thrombin-induced platelet or other cell activation, comprises administering a compound (A) comprising at least 1 segment with the amino acid sequence of formula (I) or (I'): X1-**Arg**-**Pro**-**Pro**-X2 (I) L-(X1-**Arg**-**Pro**-**PRo**-X2)n
(I') X1 = the same or different sequence of 0-30 natural or synthetic amino acid sequence; X2 = the same or different segment of 0-30 natural or synthetic amino acid sequence; L = a **linker** comprising a covalent bond or chemical group, and n= 2-20. Also claimed are: (1) a pharmaceutical composition (C1) used in the method above, and (2) a method for identifying compounds (Cs) that selectively inhibit thrombin-induced platelet and other cell activation, by measuring the ability of the

compound to bind to the thrombin cleavage site on the thrombin receptor.
USE - The method is used to inhibit ADP-induced platelet activation and aggregation in vivo (all claimed).
Dwg.0/8

L6 ANSWER 6 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1998-159541 [14] WPIDS
DNC C1998-051562
TI Thrombopoietin protein expression vector - used for increasing platelet number in a mammal.
DC B04 D16
IN IRANI, M; MORRISON-NELSON, G R; HINDU, M I
PA (ZYMO) ZYMOGENETICS INC; (ZYMO) ZYMOGENETICS
CYC 76
PI WO 9806849 A1 19980219 (199814)* EN 56p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9738238 A 19980306 (199830)
EP 920511 A1 19990609 (199927) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1230993 A 19991006 (200006)
NZ 334103 A 20000929 (200060)
MX 9901426 A1 19990801 (200063)
JP 2000516465 W 20001212 (200101) 52p
AU 728881 B 20010118 (200109)
KR 2000029998 A 20000525 (200110)
ADT WO 9806849 A1 WO 1997-US13543 19970730; AU 9738238 A AU 1997-38238 19970730; EP 920511 A1 EP 1997-935253 19970730, WO 1997-US13543 19970730; CN 1230993 A CN 1997-197984 19970730; NZ 334103 A NZ 1997-334103 19970730; MX 9901426 A1 MX 1999-1426 19990210; JP 2000516465 W WO 1997-US13543 19970730, JP 1998-509794 19970730; AU 728881 B AU 1997-38238 19970730; KR 2000029998 A WO 1997-US13543 19970730, KR 1999-701270 19990213
FDT AU 9738238 A Based on WO 9806849; EP 920511 A1 Based on WO 9806849; JP 2000516465 W Based on WO 9806849; AU 728881 B Previous Publ. AU 9738238, Based on WO 9806849; KR 2000029998 A Based on WO 9806849
PRAI US 1996-696447 19960813
AB WO 9806849 A UPAB: 19980406
A new expression vector replicable in a eukaryotic host cell comprises the following operably linked elements: (a) a transcription promoter; (b) a first DNA segment encoding a secretory leader; (c) a second segment encoding a thrombopoietin (TPO) polypeptide consisting of C-X-B, where C = a human TPO cytokine domain; X = a peptide bond or a **linker** consisting of one or two amino acid residues, such that X along in combination with C or B does not provide a dibasic amino acid pair; and B = a polypeptide consisting of residues 1 to y of the 178 amino acid sequence fragment of human TPO given in the specification, where y = an integer from 5 to 18 and up to 35% of the residues of B are individually replaced by other amino acid residues, and (d) a transcription terminator. Also claimed are: (1) a cultured eukaryotic cell, preferably a yeast cell, containing the above expression vector, and (2) a TPO polypeptide consisting of C-X-B, where C = a human TPO cytokine domain; X = a peptide bond or a **linker** consisting of one or two amino acid residues, such that X along in combination with C or B does not provide a dibasic amino acid pair; and B = a polypeptide consisting of residues 1 to y of the 178 amino acid sequence given in the specification, where y = 5-18 and at most 35% of the residues of B are individually replaced by other amino acid residues.
The vector is preferably replicable in yeast. The secretory leader is a Saccharomyces cerevisiae alpha -factor secretory leader. In B, y is

preferably at least 9. B can comprise the dipeptide Thr-Thr, or Arg-Arg. Up to 25% of the residues in B are individually replaced. Residues 1-5 of B are: **Arg-Pro-Pro**-Thr-Thr. Residue 4 of B is preferably Thr or Asp. When y is at least 10, residue 10 of B is Arg or Glu. When y is at least 14, residue 14 of B is Val or Ala. B is preferably selected from the following sequences: Ala-Pro-Pro-Thr-Thr-Ala-Val-Pro-Ser-Arg-Thr-Ser-Leu-Ala-Leu-Thr- Leu-Asn; Ala-Pro-Pro-Asp-Thr-Ala-Val-Pro-Ser-Arg-Thr-Ser-Leu-Val-Leu-Thr- Leu-Asn; etc.

USE - The host cell of (1) can be used to produce the TPO polypeptide of (2). The TPO polypeptide can be used in a method for increasing platelet number in a mammal (all claimed). The TPO polypeptide can be used to increase proliferation of bone marrow cells for treatment of cytopenia, including those induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias. It can also be used to treat thrombocytopenia, haematologic disorders, such as leukaemia and lymphoma or metastatic cancers involving bone marrow. The TPO is administered at a dose of 0.1-20 mu g/kg per day.

Dwg.0/0

L6 ANSWER 7 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1997-065304 [06] WPIDS
DNC C1997-021492
TI Inhibition of platelet activation and aggregation - by admin. of new or known bradykinin analogues.
DC B04
IN HASAN, A A K; SCHMAIER, A H
PA (UNMI) UNIV MICHIGAN
CYC 71
PI WO 9641640 A1 19961227 (199706)* EN 73p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SI SK TJ TM TR TT UA US UZ VN
AU 9663828 A 19970109 (199717)
EP 871464 A1 19981021 (199846) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 703256 B 19990325 (199924)
US 6143719 A 20001107 (200059)
JP 2001511762 W 20010814 (200154) 76p
EP 871464 B1 20030402 (200325) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69627191 E 20030508 (200338)
ADT WO 9641640 A1 WO 1996-US9940 19960607; AU 9663828 A AU 1996-63828 19960607; EP 871464 A1 EP 1996-923268 19960607, WO 1996-US9940 19960607; AU 703256 B AU 1996-63828 19960607; US 6143719 A Provisional US 1995-96P 19950609, WO 1996-US9940 19960607, US 1996-676242 19960716; JP 2001511762 W WO 1996-US9940 19960607, JP 1997-503243 19960607; EP 871464 B1 EP 1996-923268 19960607, WO 1996-US9940 19960607; DE 69627191 E DE 1996-627191 19960607, EP 1996-923268 19960607, WO 1996-US9940 19960607
FDT AU 9663828 A Based on WO 9641640; EP 871464 A1 Based on WO 9641640; AU 703256 B Previous Publ. AU 9663828, Based on WO 9641640; US 6143719 A Based on WO 9641640; JP 2001511762 W Based on WO 9641640; EP 871464 B1 Based on WO 9641640; DE 69627191 E Based on EP 871464, Based on WO 9641640
PRAI US 1995-96P 19950609; US 1996-676242 19960716
AB WO 9641640 A UPAB: 19970205
Methods for (a) inhibiting thrombin-induced activation of platelets or other cells, (b) preventing platelet aggregation and (c) inhibiting ADP-induced platelet activation comprise admin. of a peptide (I) having an amino acid sequence of formula X1-**Arg-Pro-Pro**-Gly-X2 or a multimer (II) of formula L(X1-**Arg-Pro-Pro**-Gly-X2)n, where: X1 and X2 = 0-30 natural or synthetic amino

acids; L = a **linker** comprising a covalent bond or a chemical gp.; and n = 2-20; provided that the peptide is not native bradykinin. Also claimed is a method for inhibiting thrombin-induced activation of platelets or other cells, comprising admin. of a peptide (III) having the sequence (D-Arg)-Arg-Pro-Hyp-Gly-Thi-Ser-(D-Tic)-Oic-Arg. Two specific peptides (II) are claimed as new.

USE -The methods and peptides are used to prevent arterial occlusions arising from coronary thrombosis and stroke.

ADVANTAGE - (I)-(II) are bradykinin analogues that inhibit alpha-thrombin- and ADP-induced platelet activation and secretion, inhibit alpha-thrombin-induced Ca mobilisation and prevent alpha-thrombin from cleaving its platelet receptor.

Dwg.0/11

=>

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=> s arg pro pro and branch?
           2   FILE BIOSIS
           1   FILE BIOTECHABS
           1   FILE BIOTECHDS
           4   FILE CAPLUS
           2   FILE EMBASE
  32 FILES SEARCHED...
           1   FILE ESBIOBASE
           1   FILE JICST-EPLUS
           1   FILE MEDLINE
           2   FILE SCISEARCH
         836   FILE USPATFULL
          17   FILE USPAT2
  63 FILES SEARCHED...
           3   FILE WPIDS
           3   FILE WPINDEX

    13 FILES HAVE ONE OR MORE ANSWERS,   67 FILES SEARCHED IN STNINDEX

  L1   QUE ARG PRO PRO AND BRANCH?
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YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 6 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-619166 [66] WPIDS
DNC C2002-174924
TI Novel peptide/polypeptide for cancer therapy has Fv molecule, construct or fragment, or construct of fragment with enhanced binding characteristics so as to selectively bind target cell in favor of other cells.
DC B04 B05 D16 K08
IN GUY, R; HAGAI, Y; LAZAROVITS, J; LEVANON, A; LIPSCHITZ, O; PERETZ, T; PLAKSIN, D; SZANTON, E
PA (BIOT-N) BIO-TECHNOLOGY GEN CORP
CYC 100
PI WO 2002059264 A2 20020801 (200266)* EN 232p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT WO 2002059264 A2 WO 2001-US49440 20011231
PRAI US 2000-751181 20001229
TECH UPTX: 20021014

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is produced in a eukaryotic or prokaryotic cell system, where the eukaryotic system is the mammalian cell system and the prokaryotic system comprises Escherichia coli comprising an expression vector (claimed).

Preferred Polypeptide: In (I), the first hypervariable region is a complementarity determining region 3 (CDR3) having a sequence (S) selected from Met-Arg-Ala-Pro-B-Ile, Pro-Trp-Asp-Asp-Val-Thr-Pro-Pro, Gly-Phe-Pro-Arg-Ile-Thr-Pro-Pro-Ser-Ala-Glu-Ile, Gly-Phe-Pro-Met-Pro, Gly-Phe-Pro-His-Ser-Ser-Ser-Val-Ser-Arg, Arg-Phe-Pro-Met-Arg-His-Glu-Lys-Thr-Asn-Tyr, Arg-Phe-Pro-Pro-Thr-Ala-Thr-Ile, Thr-Gln-Arg-Arg-Asp-Leu-Gly, Lys-Phe-Pro-Gly-Gly-Thr-Val-Arg-Gly-Leu-Lys, Gly-Phe-Pro-Val-Ile-Val-Glu-Glu-Arg-Gln-Ser-Thr, Arg-Phe-Pro-Gln-Arg-Val-Asp-Asn-Arg-Val, Thr-Gly-Gln-Ser-Ile-Lys-Arg-Ser, Leu-Thr-His-Pro-Tyr-Phe, Leu-**Arg-Pro-Pro**-Gln-Ser, Thr-Ser-Lys-Asn-Thr-Ser-Ser-Ser-Lys-Arg-His, Arg-Tyr-Tyr-Cys-Arg-Ser-Ser-Asp-Cys-Thr-Val-Ser, and Phe-Arg-Arg-Met-Glu-Thr-Val-Pro-Ala-Pro. The binding selectivity or specificity is secondarily influenced by a second or third hypervariable region, and/or by one or more of the upstream or downstream region flanking the first, the second and/or the third hypervariable regions. (I) is a scFv having a sequence of 277 amino acids fully defined in the specification, in which the first hypervariable region is a CDR3 region which is identical to Met-Arg-Ala-Pro-Pro-Ile. The scFv molecule comprises a straight or **branched** chain spacer of 20 or fewer amino acids residues, where the spacer has a sequence of GGGGSGGGGSGGGGSGGGGS or GGGGSGGGGSGGGGS. (I) further comprises a cassette of consecutive amino acids having a sequence selected from 84 sequences fully defined in the specification, such as a sequence comprising 98 amino acids fully defined in the specification, or having at least 90% similarity with the above sequence, or its fragment, where the cassette or fragment provides a framework into which is built, inserted, attached, coupled, combined, or fused a CDR3 region having (S). (I) has enhanced binding characteristics so as to bind selectively and/or specifically to a substantially exposed and/or over-expressed binding site on or in a target cell, where the binding to the target occurs in favor of other cells on or in which the binding site is not substantially available and/or expressed. (I) binds to an unknown ligand on a first cell having a first and a second state, where

the binding is effective in the second state but is not substantially effective in the first state, and by virtue of immuno-cross-reactivity, binds specifically or selectively to a ligand on a second cell. (I) has a formula or structure A-X-B, where X is a hypervariable CDR3 region of 3-30 amino acids, and A and B are each amino acids from 1-1000 amino acids in length, and A is the amino end and B is the carboxy end. (I) comprises a binding motif which comprises an amino acid sequence of R1-XFP-R2, where R1 and R2 comprises 0-15 amino acids residues and X is either R, G or K. The target cell is an activated, excited, modified, changed, disturbed, abnormal, or diseased cell, where the diseased cell is a cancer cell.

L3 ANSWER 2 OF 6 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-112323 [12] WPIDS
DNC C2001-033372
TI Polypeptides derived from the peptide pyrrhocoricin, useful for treating fungal infections and Gram negative/positive bacterial infections.
DC B04 C03 D16
IN OTVOS, L
PA (WIST-N) WISTAR INST ANATOMY & BIOLOGY
CYC 23
PI WO 2000078956 A1 20001228 (200112)* EN 73p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 2000060528 A 20010109 (200122)
EP 1194548 A1 20020410 (200232) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000078956 A1 WO 2000-US16989 20000621; AU 2000060528 A AU 2000-60528 20000621; EP 1194548 A1 EP 2000-946829 20000621, WO 2000-US16989 20000621
FDT AU 2000060528 A Based on WO 200078956; EP 1194548 A1 Based on WO 200078956
PRAI US 1999-154135P 19990915; US 1999-140606P 19990623
AB WO 200078956 A UPAB: 20010302
NOVELTY - Polypeptides derived from the peptide pyrrhocoricin, are new. The polypeptides are of the formula (F1) (given below or in the specification). Pyrrhocoricin is a glycopeptide characterized by the presence of a disaccharide in the mid-chain position.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a peptide of formula (F1);

(2) a composition (COMP) comprising polypeptides of formula (F1);

(3) an isolated nucleic acid molecule (NAM) comprising a nucleotide sequence encoding a peptide of formula (F) or the multi-peptide composition (COMP) in operative association with a regulatory sequence directing the expression of it in a host cell;

(4) a host cell transfected or transformed with (NAM);

(5) a method (METH1) of treating a mammalian infection comprising administering a composition comprising a peptide of formula (F1);

(6) a method for designing pharmaceutical compounds, comprising employing a peptide of formula (F1) or composition (COMP) comprising it, in a computer modelling program to design a compound which mimics the structure and/or biological effect of the peptide or composition;

(7) a method (METH2) for identifying compounds comprising:

(a) performing a competitive assay with a microorganism (which is susceptible to a peptide of formula (F1) or a composition (COMP) comprising it), a peptide of formula (F1) or a composition (COMP) comprising it and at least 1 test compound;

(b) identifying one test compound which competitively displaces the binding of the peptide or the composition to a receptor on the microorganism; and

(8) a product identified by (METH2).

R1-Asp-Lys-Gly-X-Y-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-X'-Y'-R2 (F1)

R1 = a positive charge group;

R2 = a free hydroxyl, an amide, an imide, a sugar and/or a sequence of up to 15 additional amino acids, optionally substituted with a free hydroxyl, an amide, an imide and/or a sugar (the additional amino acids are independently selected from L-configuration or D-configuration and the additional amino acids are capable of cyclizing the peptide by bridging the N- and C-termini of it);

X and Y = form a dipeptide selected from Ser-Tyr, and a dipeptide formed of naturally occurring amino acids or unnatural amino acids (the dipeptide is resistant to cleavage); and

X' and Y' = form a dipeptide selected from Asn-Arg, and a dipeptide formed of naturally occurring amino acids or unnatural amino acids (the dipeptide is resistant to cleavage).

ACTIVITY - Antibacterial; fungicidal.

A peptide comprising the sequence **Arg-Pro-Pro**-Thr-Pro-Arg-Pro-Leu-Lys-Val- was found to have an IC50 (in micro M) of 80 against Micrococcus luteus and 10 against Agrobacterium tumefaciens.

MECHANISM OF ACTION - Unknown (pyrrhocoricin binds to an unknown, stereospecific microbial target molecule).

USE - The pyrrhocoricin peptides of formula (F1) are used to treat fungal infections and bacterial infections caused by Gram-negative and Gram positive bacteria (i.e. (METH1)) (claimed).

ADVANTAGE - The polypeptide (F1) has metabolic stability in mammalian serum (claimed).

The presence of the sugar molecule in the peptide decreases the in vitro activity of the pyrrhocoricin.

Dwg.0/3

TECH UPTX: 20010302

TECHNOLOGY FOCUS - BIOLOGY - Isolation: Pyrrhocoricin may be isolated from species of Pyrrhocoris.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Polypeptides: R1 and R2 form an amino acid spacer of more than 3 amino acid residues. The spacer duplicates at least a portion of (F1).

The polypeptide (F1) has metabolic stability in mammalian serum.

At least 1 conventional amide bond between 2 amino acids in the sequence is replaced with a non-cleavable bond (such as a thio-amide bond or a reduced amide bond).

Preferred Compositions: (COMP) Comprises at least 2 polypeptides, and the second polypeptide is attached to any amino acid of the first peptide and/or any amino acid of other polypeptides in the composition.

Preferably, (COMP) comprises at least 2 polypeptides at least 1 of which is attached to a carrier. The additional polypeptide(s) is/are attached to a **branched** construct of the other polypeptide in the composition. (COMP) Preferably comprises at least 2 polypeptides of formula (F1) and each additional polypeptide is covalently linked to R2 of another peptide in the composition. (COMP) may comprise a multiple antigenic polypeptide, preferably one comprising a beta-alanine substituent on a polylysine core.

In particular, (COMP) comprises the structure (F2):

Peptide = a peptide of formula (F3).

F4 = Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn.

Preferably, (COMP) comprises the multipeptide construct (F5):

One or more of the peptides is a synthetic peptide fused to a second group which enhances the bioavailability of the peptide.

Preparation: The polypeptides in (COMP) are produced either synthetically or recombinantly.

Preferred Method: (METH1) Is used to treat fungal infections and bacterial infections caused by Gram-negative and Gram positive bacteria. (METH1) comprises administering a low dose of a composition (i.e. (COMP)) comprising deglycosylated pyrrhocoricin.

In (METH2) the microorganism may be a bacteria or a fungus.

L3 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
AN 2000:394598 CAPLUS
DN 133:208174
TI Synthesis of different types of dipeptide building units containing N- or C-terminal arginine for the assembly of backbone cyclic peptides
AU Schumann, C.; Seyfarth, L.; Greiner, G.; Reissmann, S.
CS Friedrich-Schiller-Universitat Jena, Institut fur Biochemie und Biophysik, Jena, D-07743, Germany
SO Journal of Peptide Research (2000), 55(6), 428-435
CODEN: JPERFA; ISSN: 1397-002X
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Different types of dipeptide building units contg. N- or C-terminal arginine were prepd. for synthesis of the backbone cyclic analogs of the peptide hormone bradykinin (BK: **Arg-Pro-Pro**-Gly-Phe-Ser-Pro-Phe-Arg). For cyclization in the N-terminal sequence, N-carboxyalkyl and N-aminoalkyl functionalized dipeptide building units were synthesized. To avoid lactam formation during the condensation of the N-terminal arginine to the N-alkylated amino acids at position 2, the guanidino function has to be deprotected. Best results were obtained by coupling Z-Arg(Z)2-OH with [(Me2N)2CF]PF6/collidine in CH2Cl2. Another dipeptide building unit with an acylated reduced peptide bond contg. C-terminal arginine was prepd. to synthesize BK-analogs with backbone cyclization in the C-terminus. To achieve complete condensation to the resin and to avoid side-reactions during activation of the arginine residue, this dipeptide unit was formed on a hydroxycrotonic acid linker. HYCRAM technol. was applied using the Boc-Arg(Alloc)2-OH deriv. and the Fmoc group to protect the aminoalkyl function. The reduced peptide bond was prepd. by reductive alkylation of the arginine deriv. with the Boc-protected amino aldehyde, derived from Boc-Phe-OH. The best results for condensation of the **branching** chain to the reduced peptide bond were obtained using mixed anhydrides. Both types of dipeptide building units can be used in solid-phase synthesis in the same manner as amino acid derivs.

L3 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:331364 CAPLUS
DN 129:4874
TI Preparation of bradykinin antagonists with extended hydrophobic side chains
IN Goodfellow, Val S.; Kroona, Heather B.; Whalley, Eric T.; Wincott, Francine E.; Zummach, Dana A.
PA Cortech, Inc., USA
SO U.S., 15 pp., Cont. of U.S. Ser. No. 77,998, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5750506	A	19980512	US 1996-647281	19960513
PRAI US 1993-77998		19930618		

OS MARPAT 129:4874
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Bradykinin receptor antagonists I [X = O, CH2O, S, CH2S; AA1 = D-Phe, D-1,2,3,4-tetrahydroisoquinoline-2-carboxylic acid (Tic), D-(2-indanyl)glycine, D-(cyclopentyl)glycine (Cpg) , D-Hyp, substituted

Pro; AA2 = L-octahydroinidole-2-carboxylic acid (Oic), L-Cpg, Leu, Phe, (un)substituted Pro; AA3 = L-Arg or pharmaceutical equiv.; R = H, Ac, D-Arg-Arg-Pro-Hyp-AA4, D-Arg-**Arg-Pro-Pro**-Gly-AA4, D-Arg-ARG-NHCH2(CH2)nCO; AA4 = L-thienylalanine, Phe; Z = (un)substituted pyrrolidinone, prenyl, (un)**branched** alkyl, alkenyl, alkylaryl, aryl; X = (CH2)mCONHZ, (CH2)mNHCOZ; m = 0-5; n = 0-20] which have an extended hydrophobic side chain at Cys6 are described. Thus, S-alkylation of H-D-Arg-Arg-Pro-Hyp-Gly-Phe-Cys-D-Phe-Leu-Arg-OH with dodecyl bromide gave in NH3-THF gave the corresponding S-dodecyl analog (II). II showed pA2 = 7.3 .+-. 0.10 in a bradykinin antagonist assay. with 0% recovery.

L3 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
AN 1996:326819 CAPLUS
DN 125:53896
TI Isolation and cardiovascular activity of a second bradykinin-related peptide ([Arg0,Trp5,Leu8]bradykinin) from trout
AU Conlon, J. Michael; Le Mevel, Jean-Claude; Conklin, Daniel; Weaver, Leroy; Duff, Douglas W.; Olson, Kenneth R.
CS Regulatory Peptide Center, Creighton University School Medicine, Omaha, NE, 68178, USA
SO Peptides (Tarrytown, New York) (1996), 17(3), 531-537
CODEN: PPTDD5; ISSN: 0196-9781
PB Elsevier
DT Journal
LA English
AB Previous work has shown that incubation of heat-denatured plasma from the rainbow trout Oncorhynchus mykiss with porcine pancreatic kallikrein generates [Lys0,Trp5,Leu8]bradykinin (trout[Lys0]BK). The authors have now isolated a second BK-related peptide from kallikrein-treated trout plasma with the primary structure: Arg-**Arg-Pro-Pro**-Gly-Trp-Ser-Pro-Leu-Arg (trout [Arg0]BK). Bolus injections of both trout [Arg0]BK and [Lys0]BK (>100 pmol/kg) into the dorsal aorta of conscious trout produced multi-phasic effects on arterial blood pressure. An initial pressor response of short duration (1-2 min) was followed by a fall in pressure (to below basal values in 11 out of 15 animals) and then by a sustained rise in pressure lasting up to 60 min. The max. rise in pressure produced by trout [Arg0]BK(10 nmol/kg) was approx. one-fourth of the max. rise produced by angiotensin II in the same animals. Intracerebroventricular injections of trout [Arg0]BK (500 pmol) into conscious trout had no effect on arterial blood pressure or heart rate. Trout [Arg0]BK did not affect the tension of vascular rings form trout efferent **branchial** and celiacomesenteric arteries and anterior cardinal vein. Trout des[Arg9]BK had no effect on cardiovascular parameters, either in vivo or in vitro, indicating that the C-terminal arginine residue of the peptide is important in interaction with the trout kinin receptor(s).

L3 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
AN 1990:572426 CAPLUS
DN 113:172426
TI Preparation of antithrombotic proline-containing peptideamides
IN Kawasaki, Koichi; Iwamoto, Masahiro
PA Daiichi Seiyaku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 02115197	A2	19900427	JP 1988-265809	19881021

PRAI JP 1988-265809 19881021
OS MARPAT 113:172426
AB H-X-Pro-Y-Z-NR1R2 [I; X = Gly, .beta.-Ala; Y = Arg, Lys, Orn; Z = bond, Pro, Pro-Pro; R1, R2 = H, straight chain or **branched** (cyclo)alkyl, aryl, NH2; or NR1R2 = Q; R3, R4 = H, alkyl, OH, CO2H, alkoxycarbonyl, CONH2, alkylaminocarbonyl; m, n = 0-5], having higher antithrombotic activity than the N-terminus .alpha.-chain of fibrin, are prepd. Thus, deprotection of p-MeOC6H4CH2O2C-Arg(NO2)-Pro-NEt2 (prepn. given) with CF3CO2H in anisole followed by condensation with BOC-Gly-Pro-OH in the presence of Me2CHCH2O2CCl and Et3N in DMF gave BOC-Gly-Pro-Arg(NO2)-Pro-NEt2. Deprotection of the latter by hydrogenolysis over Pd and treatment with 6N aq. HCl/dioxane under ice-cooling gave H-Gly-Pro-Arg-Pro-NEt2 (II). A total of 11 I and their salts were prepd. II and H-Gly-Pro-**Arg**-**Pro**-**Pro**-NH2 were 5.7 times more potent than H-Gly-Pro-Arg-Pro-OH in inhibiting thrombin-induced coagulation of fibrinogen.

L15 ANSWER 37 OF 52 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1979:551761 CAPLUS
DN 91:151761
TI Effect of bradykinin on platelet aggregation
AU Markosyan, R. A.; Suvorov, A. V.
CS All-Union Res. Cardiol. Cent., Moscow, USSR
SO Byulleten Eksperimental'noi Biologii i Meditsiny (1979), 88(8), 139-41
CODEN: BEBMAE; ISSN: 0365-9615
DT Journal
LA Russian
AB **ADP**-induced **aggregation** of rabbit platelets was max. inhibited by preincubation of the platelets for 5-10 min with 10 ng **bradykinin** [58-82-2]/mL. **Bradykinin** also inhibited canine **platelet aggregation**.

18 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **58-82-2** REGISTRY
CN Bradykinin (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Arginine, N2-[N-[1-[N-[N-[N-[1-(1-arginyl-L-prolyl)-L-prolyl]glycyl]-3-phenylalanyl]seryl]prolyl]-3-phenylalanyl]- (6CI)
OTHER NAMES:
CN 13: PN: WO0023092 SEQID: 13 unclaimed sequence
CN 147: PN: US20030119021 SEQID: 25 unclaimed sequence
CN 14: PN: US6525021 SEQID: 13 unclaimed sequence
CN 15: PN: US6258776 SEQID: 24 unclaimed sequence
CN 1: PN: WO02102835 SEQID: 3 unclaimed sequence
CN 3: PN: WO02059343 SEQID: 3 unclaimed sequence
CN 41: PN: WO03028666 SEQID: 38 unclaimed sequence
CN 6: PN: US6395513 SEQID: 9 unclaimed sequence
CN 6: PN: WO0112656 SEQID: 47 unclaimed sequence
CN BRS 640
CN Callidin I
CN Kallidin 9
CN Kallidin I
CN L-Arginine, L-arginyl-L-prolyl-L-prolylglycyl-L-phenylalanyl-L-seryl-L-prolyl-L-phenylalanyl-
CN L-Bradykinin
CN Synthetic bradykinin
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 9

PATENT ANNOTATIONS (PNTE):

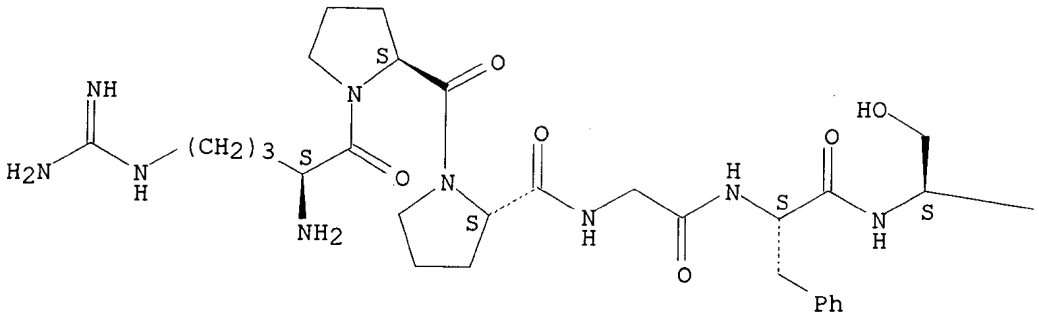
Sequence Source	Patent Reference
Not Given	US6258776 unclaimed SEQID 24
	US6395513 unclaimed SEQID 9
	WO2000023092 unclaimed SEQID 13
	WO2001012656 unclaimed SEQID 47

SEQ 1 RPPGFSPFR

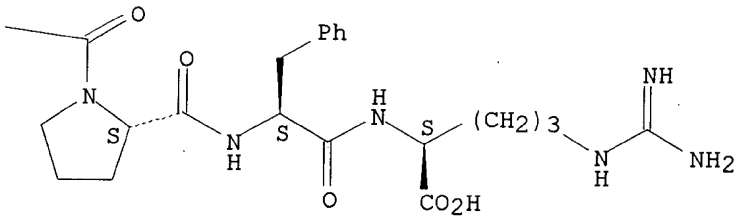
RELATED SEQUENCES AVAILABLE WITH SEQLINK
DR 9008-50-8
MF C50 H73 N15 O11
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



10088 REFERENCES IN FILE CA (1937 TO DATE)
340 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10103 REFERENCES IN FILE CAPLUS (1937 TO DATE)
82 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 9
AN 1993:622626 CAPLUS
DN 119:222626
TI Inhibitory effects of enzymic hydrolyzates of collagen and collagen-related synthetic peptides on fibrinogen/thrombin clotting
AU Maruyama, Susumu; Nonaka, Isao; Tanaka, Hideoki
CS Natl. Inst. Biosci. Hum.-Technicol., Agency Ind. Sci. Technol., Tsukuba, 305, Japan
SO Biochimica et Biophysica Acta (1993), 1164(2), 215-18
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB Inhibitory effects of some enzymic hydrolyzates of collagen and collagen-related synthetic peptides on fibrinogen/**thrombin** clotting were investigated. The hydrolyzate of porcine skin collagen with thermolysin or bacterial collagenase inhibited fibrinogen/**thrombin** clotting, but did not inhibit the activity of **thrombin**. Although the activity was not pronounced, the hydrolyzate of collagen with such proteinases as trypsin and pepsin also inhibited the clotting. Gly-Pro-Arg, which is a known inhibitor of fibrinogen/**thrombin** clotting, was isolated from the bacterial collagenase hydrolyzate of porcine collagen by HPLC. Collagen-related synthetic peptides such as Gly-Pro-Arg-Gly, Gly-Pro-Arg-Gly-Pro, Gly-Pro-Arg-Gly-Pro-Ala, Gly-Pro-Arg-Gly-Pro-Pro, and Gly-Pro-**Arg-Pro-Pro** also inhibited the clotting, but did not inhibit the activity of **thrombin**. The inhibitory activity of Gly-Pro-Arg-Gly-Pro-Pro and Gly-Pro-**Arg-Pro-Pro** was more marked than that of Gly-Pro-Arg. However, Gly-Pro-Lys, Gly-Ala-Arg, Gly-Pro-Hyp, Ala-Gly-Pro-Arg and Gly-Pro-Gly-Pro-Arg had no inhibitory effect on the clotting.

RPPGTSP

L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1990:151249 CAPLUS
DN 112:151249
TI Amino acids and peptides XII: synthetic peptides related to the N-terminal portion of fibrin .alpha.-chain and their inhibitory effects on fibrinogen/thrombin clotting
AU Kawasaki, Koichi; Hirase, Katsuhiko; Tsuji, Toshiki; Miyano, Masanori; Iwamoto, Masahiro
CS Fac. Pharm. Sci., Kobe-Gakuin Univ., Kobe, 673, Japan
SO Thrombosis Research (1989), 56(6), 757-62
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
AB A series of peptides related to the N-terminal portion of the fibrin .alpha.-chain (3-7 residues) and peptide amide analogs was prepd. by methods yet to be published, and tested for their ability to inhibit fibrinogen/**thrombin** clotting (presumably by binding to fibrinogen rather than **thrombin**). Among the tripeptide analogs, bulky secondary amine component of the C-terminal amide tended to increase the inhibitory effect. The most effective inhibitor was the pentapeptide amide H-Gly-Pro-**Arg**-**Pro**-**Pro**-NH2. Studies with tetrapeptides revealed the importance of Gly, L-Pro, and L-Arg in the N-terminal position. H-Gly-Pro-Arg-amide analogs prepd. from secondary amines were approx. as good as their corresponding tetrapeptides.

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L11 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1998:265647 CAPLUS
DN 129:28198
TI Structure and property of model peptides of proline/arginine-rich region in bactenecin 5
AU Niidome, Takuro; Mihara, Hisakazu; Oka, Masahito; Hayashi, Toshio; Saiki, Tetsunobu; Yoshida, Kazutoshi; Aoyagi, Haruhiko
CS Department of Applied Chemistry, Faculty of Engineering, Nagasaki University, Nagasaki, Japan
SO Journal of Peptide Research (1998), 51(5), 337-345
CODEN: JPERFA; ISSN: 1397-002X
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 123938-69-2P, Bactenecin 5 (cattle) **189395-82-2P** 189395-83-3P
189395-84-4P 189519-11-7P 189519-14-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(mol. structure, antibacterial activity and conformation of model peptides of proline/arginine-rich region in bactenecin-5)
IT **207804-27-1** 207804-28-2 207868-82-4 207868-85-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(mol. structure, antibacterial activity and conformation of model peptides of proline/arginine-rich region in bactenecin-5)
IT 207804-23-7P 207804-24-8P **207804-25-9P 207804-26-0P**
207804-29-3P 207868-86-8P 207868-89-1P 207927-22-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(mol. structure, antibacterial activity and conformation of model peptides of proline/arginine-rich region in bactenecin-5)

L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1997:343667 CAPLUS
DN 126:330830
TI Structure and function of Pro/Arg-rich repeated region in antibiotic bactenecin 5
AU Niidome, Takuro; Mihara, Hisakazu; Saiki, Tetsunobu; Oka, Masahito; Aoyagi, Haruhiko
CS Department of Applied Chemistry, Faculty of Engineering, Nagasaki University, Nagasaki, 852, Japan
SO Peptide Chemistry (1996), 34th, 185-188
CODEN: PECHDP; ISSN: 0388-3698
PB Protein Research Foundation
DT Journal
LA English
IT 123938-69-2DP, Bactenecin 5, peptide models **189395-82-2P**
189395-83-3P 189395-84-4P 189519-11-7P 189519-14-0P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(structure and function of Pro/Arg-rich repeated region in antibiotic bactenecin 5)

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L27 ANSWER 5 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1986-050265 [08] WPIDS
DNC C1986-021116
TI Hypotensive compsns. contg. di tri or tetra peptide(s) - have good efficacy with low toxicity and side effects.
DC B04
IN PANG, P K; TENNER, T E
PA (UYTE-N) TEXAS TECH UNIV HEA
CYC 3
PI GB 2163166 A 19860219 (198608)* 8p
US 4585757 A 19860429 (198620)
FR 2571258 A 19860411 (198621)
ADT GB 2163166 A GB 1985-18793 19850725; US 4585757 A US 1984-635219 19840727; FR 2571258 A FR 1985-11008 19850718
PRAI US 1984-635219 19840727
ABEQ US 4585757 A UPAB: 19930922
Antihypertensive compsns. comprise a carrier and an effective amt. of a peptide having 1 of the following amino acid sequences: Pro-Arg; Lys-Arg-Pro(pref.); Pro-Lys(pref.); Arg-Arg-Pro(pref.); Pro-Arg-Arg; Arg-Lys-Pro; Pro-Lys-Lys; Pro-Pro-Arg-Arg; Pro-Arg-Lys(pref.); Pro-Pro-Arg-Lys; Pro-Lys-**Arg**; **Pro-Pro-Lys**-Lys; Pro-Pro-**Arg**; **Pro-Pro-Lys-Arg**; **Pro-Pro-Lys**; Arg-**Arg-Pro-Pro**; **Lys**-Pro-Pro; Lys-Lys-Pro-Pro; Lys-Lys-Pro; Arg-Lys-Pro-Pro; or Lys-Arg-Pro-Pro(pref.). Peptides are synthesised by known methods.

AN 1996:519830 CAPLUS
DN 125:186614
TI Bradykinin and its metabolite, Arg-Pro-Pro-Gly-Phe, are selective inhibitors of .alpha.-thrombin-induced platelet activation
AU Hasan, Ahmed A. K.; Amenta, Styliani; Schmaier, Alvin H.
CS Department Internal Medicine, University Michigan, Ann Arbor, MI, 48109-0724, USA
SO Circulation (1996), 94(3), 517-528
CODEN: CIRCAZ; ISSN: 0009-7322
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB Plasma kininogens are selective inhibitors of .alpha.-thrombin activation of platelets and endothelial cells. In the present study, we localized the .alpha.-thrombin inhibitory sequence of kininogens and describe its mechanism of action. Bradykinin and an analog, MKRPPGFSPFRSSRIG, inhibited .alpha.-thrombin-induced platelet aggregation and secretion with an IC50 of 0.25 and 1 mmol/L and of 0.23 and 0.5 mmol/L, resp. The minimal inhibitory peptide was RPPGF. Bradykinin and its analogs did not inhibit ADP-, collagen-, U46619-, or SFLLRN-induced platelet activation or the ability of .alpha.-thrombin to cleave chromogenic substrates, clot fibrinogen, or block .alpha.-thrombin binding to platelets. Bradykinin , MKRPPGFSPFRSSRIG, and RPPGF abolished .alpha.-thrombin-induced (1 nmol/L) calcium mobilization. On flow cytometry, bradykinin and MKRPPGFSPFRSSRIG blocked .alpha.-thrombin from removing the epitope of its cleavage site on the cloned thrombin receptor. Furthermore, peptide RPPGF or high-mol.-wt. kininogen prevented .alpha.-thrombin from cleaving the thrombin receptor peptide, NATLDPRSFLLR, between arginine and serine. These results indicate that bradykinin and its metabolites are selective antithrombins by preventing .alpha.-thrombin cleavage of the cloned thrombin receptor between arginine-41 and serine-42. These newly recognized antithrombin peptides, which are termed thrombostatins, contribute to the cardioprotective nature of kinins.
ST bradykinin alpha thrombin platelet
IT Blood platelet
(bradykinin and metabolite inhibition of .alpha.-thrombin action on blood platelets)
IT Nomenclature, new natural products
(thrombostatin)
IT Receptors
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(thrombin, bradykinin and metabolite inhibition of .alpha.-thrombin-induced cleavage of receptor on blood platelets)
IT 23815-89-6
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(as bradykinin metabolite and its inhibition of .alpha.-thrombin action on blood platelets)

IT 181057-49-8
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(bradykinin and metabolite)

IT 9002-04-4, Thrombin
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(bradykinin and metabolite and inhibition of .alpha.-thrombin action on blood platelets)

IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(bradykinin and metabolite inhibition of .alpha.-thrombin-induced Ca mobilization in relation to action on blood platelets)

IT 58-82-2, Bradykinin 180895-14-1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(inhibition of .alpha.-thrombin action on blood platelets)